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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/502,256 | 07/23/2004 | Takehiko Kitamori | 2004_1163A | 3964 |
| 513 7590 01/09/2006 WENDEROTH, LIND & PONACK, L.L.P. 2033 K STREET N. W. SUITE 800 WASHINGTON, DC 20006-1021 | | | EXAMINER LUM, LEON YUN BON | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1641 | |

DATE MAILED: 01/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/502,256

Applicant(s)

KITAMORI ET AL.

Examiner

Leon Y. Lum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 October 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The amendment filed 25 October 2005 is acknowledged and has been entered.

Information Disclosure Statement

2. The information disclosure statement filed 25 October 2005 will not be signed since it does not contain references that were not previously considered. Both foreign patent documents listed therein were considered and indicated as such on the IDS form mailed on 25 May 2005.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. In claim 21, line 10, the phrase "antigen antibody" is vague and indefinite. It is unclear whether the phrase should be "antigen or antibody" or "antigen/antibody". Is

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just one of either the antigen or antibody reacting with the enzyme (line 11) or is an antigen/antibody complex reacting with the enzyme?

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claim 20 is rejected under 35 U.S.C. 102(e) as being anticipated by Harrison et al (US 6,432,290 B1).

Harrison et al reference teaches a microfluidic substrate (i.e. enzyme immunoassay chip) with buffer inlets 33 and 33a leading into a chamber (i.e. reaction liquid leading-in flow passage part), trapping zone 35 and exit channel 37 (i.e. reaction flow passage part), and collection channel 40 (i.e. detection flow passage part), wherein the chambers and channels are fluidly connected in sequence (i.e. successively connected with each other). See column 17, line 39 to column 18, line 7; and Figure 9. In addition, Harrison et al teach that trapping zone 35 includes side channel 34 that pack and unpack the zone with solid phase extraction material (i.e. inlet part for bead-bodies), and that weir 6f in between trapping zone 35 and exit channel 37 (i.e. flow

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stopping part). See column 17, lines 55-67 and Figure 9. Furthermore, Harrison et al teach that beads are unable to traverse the weirs because the distance from the top of the weirs to the bottom of the plate is less than the diameter of the individual particles (i.e. flow stopping part has a channel depth shallower than that of the reaction flow passage to stop the flow of bead-bodies through the reaction flow passage part). See column 8, lines 56-61 and Figures 2A and 3A. Harrison et al also teach that the solid phase extraction material in zone 35 are beads with antibody on the surface that react with antigen in solution (i.e. bead-bodies with antibodies fixed thereon). See column 12, lines 35-40.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harrison et al (US 6,432,290 B1) in view of Eteshola et al (Sensors and Actuators B, 2001) and Sato et al (Analytical Sciences, 1999).

Harrison et al reference has been disclosed above, and additionally teaches a method of detecting light generated from an enzyme reaction, wherein the detection is downstream from the enzyme bed (i.e. enzyme reaction products are detected in the detection flow passage part). See column 13, lines 4-7; and column 13, line 64 to column 14, line 4. However, Harrison et al fail to teach that the enzyme reaction product is produced by antigen antibody reaction with an enzyme, wherein the enzyme is in solution and the antigen antibody reaction is on bead-bodies. In addition, Harrison

et al fail to teach detection by a thermal lens microscope system in the detection flow passage part.

Eteshola et al teach the downstream detection of a fluorophore in a microfluidic device, wherein the fluorophore is generated from an HPR-catalyzed fluorogenic substrate conversion, in order to provide a fast, simply, and sensitive immunoassay that does not require a multistate, labor-intensive process with long incubation periods and washes. See page 129, left column, 2nd paragraph to right column, 1st paragraph; and page 130, right column, 3rd paragraph to page 131, left column, 1st paragraph; and Figure 1 and caption.

Sato et al teach a thermal-lens microscope to detect optical irradiation in a microfluidic channel, in order to provide a means of optical detection with ultrahigh sensitivity and stability. See page 526, left column, 1st paragraph to right column, 1st paragraph; and Figure 1 and caption. In addition, Sato et al teach applications of the thermal-lens microscope to enzyme and immunoassays. See page 525, left column, 2nd paragraph,

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus and method of Harrison et al with the downstream detection of a fluorophore in a microfluidic device, wherein the fluorophore is generated from an HPR-catalyzed fluorogenic substrate conversion, as taught by Eteshola et al, in order to provide a fast, simply, and sensitive ELISA that does not require a multistate, labor-intensive process with long incubation periods and washes. The efficiency of HPR-catalyzed fluorogenic substrate conversion, as taught by Eteshola, provides the

motivation to combine the mobile enzyme and immobilized antibody technique of Eteshola with the method of Harrison et al. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the downstream detection of a fluorophore in an ELISA, as taught by Eteshola et al, in the apparatus and method of Harrison et al, since Harrison et al teach a microfluidic device with antigen capture for immunoassays and downstream detection, and the fluorophore production and detection of Eteshola et al is also in a microfluidic device with antigen capture and means for downstream detection.

It would also have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Harrison et al with a thermal-lens microscope to detect optical irradiation in a microfluidic channel, as taught by Sato et al, in order to provide a means of optical detection with ultrahigh sensitivity and stability. The effectiveness of the thermal-lens microscope, as taught by Sato et al, provides motivation to combine the microscope with the detection method of Harrison et al. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a thermal lens microscope, as taught by Sato et al, in the apparatus of Harrison et al, since Harrison et al teach a detection channel and detection means to detect enzyme reactions that give off light, and the thermal lens microscope of Sato et al performs detection by through optical irradiation of enzyme reactions.

Response to Arguments

12. On pages 6-7 of the Remarks, Applicants argue that the applied references do not teach the claimed invention. Specifically, Applicants four points:

(1) Applicants contend that Harrison “fails to disclose or suggest a reaction flow passage part which consists of an inlet part for bead-bodies with antibodies fixed thereon, a flow stopping part for the bead-bodies and an area between the inlet part for the bead-bodies and the flow stopping part.” See page 6, 7th paragraph of the Remarks.

(2) Applicants also argue that Harrison reference “adds to the technical problem of the prior art” because the beads do not “contribute to the increase of signal strength” and “Nor do the majority of elution of fluorescent labeled reagents reach the detector”. See page 7, 3rd paragraph of the Remarks.

(3) Applicants also state that the Harrison structure is different from the claimed invention because at least one side channel connected with the chamber is indispensable since it supplies beads to the chamber between at least one pair of weirs. See page 7, 4th paragraph of the Remarks.

(4) Lastly, Applicants argue that Harrison fails to disclose or suggest that the enzyme reaction product is produced by antigen antibody reaction with an enzyme, and that the secondary references also fail to teach this limitation. See page 7, 5th-6th paragraphs of the Remarks.

Applicants' arguments have been fully considered, but are not persuasive. Regarding the first point above, Harrison reference does in fact teach the claimed "reaction flow passage part which consists of an inlet part for bead-bodies with antibodies fixed thereon, a flow stopping part for the bead-bodies and an area between the inlet part for the bead-bodies and the flow stopping part." This arrangement is especially evident in Figure 9 and its corresponding description in columns 17-18.

Regarding the second point above, Applicant statements that (1) the beads of Harrison do not contribute to increase of signal strength and (2) that the majority of fluorescent reagents do not reach the detector are not given patentable weight since these situations are not claimed. Although claim 21 is a method claim, it does not contain language that would even suggest that the bead-bodies as claimed are required to provide increased signal strength and that a majority of fluorescent reagents reach the detector.

Regarding the third point above, it is unclear what Applicants mean by a side channel that is "indispensable" and how this would constitute a distinction between the Harrison reference and the instant invention. The claimed chip simply requires an arrangement of chambers and channels, all of which have been described above as being disclosed by Harrison and properly teach the claimed arrangement. The intended use of the chip is to supply beads from an inlet part into a reaction flow passage part, where it is stopped by a flow stopping part. The arrangement taught by Harrison provides for this intended use since inlet 34 (i.e. inlet part) provides antibody-immobilized beads into channel 35, which is fluidly connected to channel 37 and

separated therefrom by weir 6f (i.e. flow stopping part). Channels 35 and 37 are considered to be one continuous channel that is separated by weir 6f, thereby reading on the limitation of a reaction flow passage part with a flow stopping part therein. Therefore, antibody-immobilized beads enter channel 35 through inlet 34 and are stopped from moving down the continuous channel and into portion 37 by weir 6f. Since Harrison teaches the claimed structures and their capability to perform the cited intended use, Harrison is properly applied.

Regarding Applicants' fourth point above, Harrison reference is not relied upon to teach the claimed limitations. Contrary to Applicants' statements, Eteshola reference is applied to teach that the claimed enzyme reaction product is produced by antigen antibody reaction with an enzyme. See above rejection.

In light of the above statements, Applicants' arguments are thereby not considered to be persuasive.

Conclusion

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

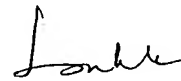
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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leon Y. Lum
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01/04/06